

**AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions and listings of claims in the application.

Claim 1 (previously presented): A composition comprising an isolated immunostimulatory sequence (ISS), and a pharmaceutically acceptable excipient wherein the ISS is less than about 200 nucleotides in length and comprises the formula:

5'-X<sub>1</sub> X<sub>2</sub> A X<sub>3</sub> C G X<sub>4</sub> T C G-3' (SEQ ID NO: 62)

wherein X<sub>1</sub> is T, G, C or Z, wherein Z is 5-bromocytosine;

wherein X<sub>2</sub> is T, G, A or U;

wherein X<sub>3</sub> is T, A or C;

wherein X<sub>4</sub> is T, G or U; and

wherein the ISS is not 5'-TGAACGTTTCG-3' (SEQ ID NO: 63) or 5'-GGAACGTTTCG-3' (SEQ ID NO: 64).

Claim 2 (previously presented): The composition according to claim 1, wherein the ISS is selected from the group consisting of TGAACGUTCG (SEQ ID NO: 67), TGACCGTTTCG (SEQ ID NO: 68), TGATCGGTCG (SEQ ID NO: 69), TGATCGTTTCG (SEQ ID NO: 70), TGAACGGTCG (SEQ ID NO: 71), GTAACGTTTCG (SEQ ID NO: 72), GTATCGGTCG (SEQ ID NO: 73), GTACCGTTTCG (SEQ ID NO: 74), GAACCGTTTCG (SEQ ID NO: 75), ZGACCGTTTCG (SEQ ID NO: 76), wherein Z is 5-bromocytosine, CGAACGTTTCG (SEQ ID NO: 77), CGACCGTTTCG (SEQ ID NO: 78), ZGAACGTTTCG (SEQ ID NO: 79), wherein Z is 5-bromocytosine, TTAACGUTCG (SEQ ID NO: 80), TUAACGUTCG (SEQ ID NO: 81) and TTAACGTTTCG (SEQ ID NO: 82).

Claim 3 (previously presented): The composition according to claim 2, wherein the ISS is selected from the group consisting of TGAACGUTCG (SEQ ID NO: 67), GAACCGTTTCG (SEQ ID NO: 75) and CGAACGTTTCG (SEQ ID NO: 77).

Claim 4 (previously presented): The composition according to claim 3 comprising a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 18, SEQ ID NO: 19 and SEQ ID NO: 132.

Claim 5 (withdrawn): An immunomodulatory polynucleotide comprising an immunostimulatory sequence (ISS), wherein the ISS comprises the formula:

5'-X<sub>1</sub> X<sub>2</sub> A X<sub>3</sub> Z G X<sub>4</sub> T C G-3' (SEQ ID NO: 65)

wherein Z is 5-bromocytosine;

wherein X<sub>1</sub> is T, G, C or Z, wherein Z is 5-bromocytosine;

wherein X<sub>2</sub> is T, G, A or U;

wherein X<sub>3</sub> is T, A or C;

wherein X<sub>4</sub> is T, G or U; and

wherein the ISS is not 5'-TGAAZGTTTCG-3' (SEQ ID NO: 66), wherein Z is 5-bromocytosine.

Claim 6 (withdrawn): An immunomodulatory polynucleotide according to claim 5, wherein the ISS is selected from the group consisting of TGAAZGUTCG, (SEQ ID NO: 83) TGACZGTTTCG (SEQ ID NO: 84), TGATZGGTCG (SEQ ID NO: 85), GTATZGGTCG (SEQ ID NO: 86), GTACZGTTTCG (SEQ ID NO: 87), GAACZGTTTCG (SEQ ID NO: 88), GAAAZGUTCG (SEQ ID NO: 89), ZGACZGTTTCG (SEQ ID NO: 90), CGAAZGTTTCG (SEQ ID NO: 91), ZGAAZGTTTCG (SEQ ID NO: 92), ZGAAZGUTCG (SEQ ID NO: 93), TTAAGZGUTCG (SEQ ID

NO: 94), TAAAZGUTCG (SEQ ID NO: 95) and TTAAZGTTCG (SEQ ID NO: 96), wherein Z is 5-bromocytosine.

Claim 7 (withdrawn): An immunomodulatory polynucleotide according to claim 6, wherein the ISS is selected from the group consisting of ZGAAZGUTCG (SEQ ID NO: 93) and GAAAZGUTCG (SEQ ID NO: 89), wherein Z is 5-bromocytosine.

Claim 8 (withdrawn): An immunomodulatory polynucleotide according to claim 7 comprising a sequence selected from the group consisting of SEQ ID NO: 35 and SEQ ID NO: 36.

Claim 9 (previously presented): The composition according to claim 1, wherein the ISS further comprises at least one TCG sequence.

Claim 10 (previously presented): The composition according to claim 9, wherein the TCG sequence is adjacent to the 5' end of the ISS.

Claim 11 (previously presented): The composition according to claim 1, wherein the ISS further comprises a TCGA sequence.

Claim 12 (previously presented): The composition according to claim 1, wherein the ISS further comprises at least one T, 5-bromocytosine, G sequence.

Claim 13 (previously presented): The composition according to claim 12, wherein the T, 5-bromocytosine, G sequence is adjacent to the 5' end of the ISS.

Claim 14 (previously presented): The composition according to claim 1, wherein the ISS further comprises a T, 5-bromocytosine, G, A sequence.

Claim 15 (previously presented): The composition according to claim 1, wherein the ISS is less than about 150 bases or base pairs in length.

Claim 16 (previously presented): The composition according to claim 1, wherein the ISS is less than about 100 bases or base pairs in length.

Claim 17 (previously presented): The composition according to claim 1, wherein the ISS is less than about 50 bases or base pairs in length.

Claim 18 (previously presented): The composition according to claim 1, wherein the ISS is single-stranded.

Claim 19 (previously presented): The composition according to claim 1, wherein the ISS is double-stranded.

Claim 20 (previously presented): The composition according to claim 1, wherein the ISS is stabilized.

Claim 21 (previously presented): The composition according to claim 20, wherein the ISS comprises a phosphorothioate bond.

Claims 22-23 (cancelled)

Claim 24 (previously presented): The composition according to claim 1 further comprising an antigen.

Claim 25 (cancelled)

Claim 26 (previously presented): The composition according to claim 1, wherein the ISS is linked to a biodegradable microcarrier (MC), wherein said MC is less than 10  $\mu\text{m}$  in size.

Claim 27 (withdrawn): An immunomodulatory polynucleotide/microcarrier (IMP/MC) complex, comprising:

a polynucleotide according to claim 5 linked to a biodegradable microcarrier (MC), wherein said MC is less than 10  $\mu\text{m}$  in size.

Claim 28 (withdrawn): A method of modulating an immune response in an individual comprising administering to an individual an immunomodulatory polynucleotide according to claim 1 or claim 5 in an amount sufficient to modulate an immune response in said individual.

Claim 29 (withdrawn): The method of claim 28, wherein said individual suffers from a disorder associated with a Th2-type immune response.

Claim 30 (withdrawn): The method of claim 29, wherein said disorder associated with a Th2-type immune response is an allergy or asthma.

Claim 31 (withdrawn): The method of claim 28, wherein said individual has an infectious disease.

Claim 32 (withdrawn): A method of increasing interferon-gamma (IFN- $\gamma$ ) in an individual, comprising:

administering an immunomodulatory polynucleotide according to claim 1 or claim 5 to said individual in an amount sufficient to increase IFN- $\gamma$  in said individual.

Claim 33 (withdrawn): The method of claim 32, wherein said individual has idiopathic pulmonary fibrosis.

Claim 34 (withdrawn): A method of increasing interferon-alpha (IFN- $\alpha$ ) in an individual, comprising:

administering an immunomodulatory polynucleotide according to claim 1 or claim 5 to said individual in an amount sufficient to increase IFN-  $\alpha$  in said individual.

Claim 35 (withdrawn): The method of claim 34, wherein said individual has a viral infection.

Claim 36 (withdrawn): A method of increasing interferon-alpha (IFN-  $\alpha$ ) in an individual, comprising:

administering an immunomodulatory polynucleotide according to claim 9 to said individual in an amount sufficient to increase IFN-  $\alpha$  in said individual.

Claim 37 (withdrawn): The method of claim 35, wherein said individual has a viral infection.

Claim 38 (withdrawn): A method of increasing interferon-alpha (IFN-  $\alpha$ ) in an individual, comprising:

administering an immunomodulatory polynucleotide according to claim 11 to said individual in an amount sufficient to increase IFN-  $\alpha$  in said individual.

Claim 39 (withdrawn): The method of claim 38, wherein said individual has a viral infection.

Claim 40 (withdrawn): A method of ameliorating a symptom of an infectious disease in an individual, comprising:

administering an effective amount of an immunomodulatory polynucleotide according to claim 1 or claim 5 to the individual, wherein an effective amount is an amount sufficient to ameliorate a symptom of said infectious disease.

Claim 41 (withdrawn): The method of claim 40, wherein said infectious disease is an infectious disease caused by a cellular pathogen.

Claim 42 (withdrawn): The method of claim 41, wherein said infectious disease caused by a cellular pathogen is selected from the group consisting of mycobacterial disease, malaria, leishmaniasis, toxoplasmosis, schistosomiasis and clonorchiasis.

Claim 43 (withdrawn): A method of ameliorating a symptom of an IgE-related disorder in an individual, comprising:

administering an effective amount of an immunomodulatory polynucleotide according to claim 1 or claim 5 to an individual having an IgE-related disorder, wherein an effective amount is an amount sufficient to ameliorate a symptom of said IgE-related disorder.

Claim 44 (withdrawn): The method of claim 43, wherein said IgE-related disorder is allergy.

Claim 45 (withdrawn): The method of claim 43, wherein said IgE-related disorder is an allergy-related disorder.

Claim 46 (withdrawn): The method of claim 43, wherein said IgE-related disorder is asthma.

Claim 47 (previously presented): A kit comprising a composition according to claim 1.

Claim 48 (previously presented): The kit of claim 47, further comprising instructions for use of the composition for immunostimulation of an individual.

Claim 49 (new): A composition comprising an isolated immunostimulatory sequence (ISS), and a pharmaceutically acceptable excipient wherein the ISS is less than about 200 nucleotides in length and comprises the formula:

5'-X<sub>1</sub> X<sub>2</sub> A X<sub>3</sub> C G X<sub>4</sub> T C G-3' (SEQ ID NO: 62)

wherein X<sub>1</sub> is T, G, C or Z, wherein Z is 5-bromocytosine;

wherein X<sub>2</sub> is T, G, A or U;

wherein X<sub>3</sub> is T, A or C;

wherein X<sub>4</sub> is T, G or U; and

wherein the ISS is selected from the group consisting of 5'-TCGTCGGAACCGTTCGGAATGA-3' (SEQ ID NO: 18); 5'-TGACTGTGAAZGTTZGAGATGA-3' (SEQ ID NO: 38); and 5'-TGACTGTGAACGTTCGAGATGA-3' (SEQ ID NO: 59).

Claim 50 (new): A composition comprising an isolated immunostimulatory sequence (ISS), and a pharmaceutically acceptable excipient wherein the ISS is less than about 200 nucleotides in length and comprises the formula:

5'-X<sub>1</sub> X<sub>2</sub> A X<sub>3</sub> C G X<sub>4</sub> T C G-3' (SEQ ID NO: 62)

wherein X<sub>1</sub> is T, G, C or Z, wherein Z is 5-bromocytosine;

wherein X<sub>2</sub> is T, G, A or U;

wherein X<sub>3</sub> is T, A or C;

wherein X<sub>4</sub> is T, G or U; and

wherein the ISS is selected from the group consisting of: SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 33, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 55, SEQ ID NO: 59, and SEQ ID NO: 60.



Claim 51 (new): A composition comprising an isolated immunostimulatory sequence (ISS), and a pharmaceutically acceptable excipient wherein the ISS is less than about 200 nucleotides in length and comprises the formula:



wherein  $X_1$  is T, G, C or Z, wherein Z is 5-bromocytosine;

wherein  $X_2$  is T, G, A or U;

wherein  $X_3$  is T, A or C;

wherein  $X_4$  is T, G or U; and

wherein the ISS is selected from the group consisting of: SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 55, SEQ ID NO: 59, SEQ ID NO: 60.

Claim 52 (new): A composition comprising an isolated immunostimulatory sequence (ISS), and a pharmaceutically acceptable excipient wherein the ISS is less than about 200 nucleotides in length and comprises the formula:



wherein  $X_1$  is T, G, C or Z, wherein Z is 5-bromocytosine;

wherein  $X_2$  is T, G, A or U;

wherein X<sub>3</sub> is T, A or C;

wherein X<sub>4</sub> is T, G or U; and

wherein the ISS is selected from the group consisting of: SEQ ID NO: 2, SEQ ID NO: 18, SEQ ID NO: 35, SEQ ID NO: 38, SEQ ID NO: 59, SEQ ID NO: 60.

Claim 53 (new): A composition comprising an isolated immunostimulatory sequence (ISS), and a pharmaceutically acceptable excipient wherein the ISS is less than about 200 nucleotides in length and comprises the formula:

5'-X<sub>1</sub> X<sub>2</sub> A X<sub>3</sub> C G X<sub>4</sub> T C G-3' (SEQ ID NO: 62)

wherein X<sub>1</sub> is T, G, C or Z, wherein Z is 5-bromocytosine;

wherein X<sub>2</sub> is T, G, A or U;

wherein X<sub>3</sub> is T, A or C;

wherein X<sub>4</sub> is T, G or U; and

wherein the ISS is selected from the group consisting of: SEQ ID NO: 1, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 132.